Biomedical Research 2017; 28 (12): 5580-5582 *ISSN 0970-938X*
www.biomedres.info

MiR-196a2 rs11614913 polymorphism could not influence coronary artery disease risk in Asians.

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Abstract

Although some studies have investigated the association between miR-196a2 rs11614913 polymorphism and coronary artery disease (CAD) risk. The effect of miR-196a2 rs11614913 polymorphism on CAD susceptibility remain unknown. This meta-analysis aimed to determine this association. PubMed and EMBASE were searched to find relevant studies which investigated the association between miR-196a2 rs11614913 polymorphism and CAD risk. Five case-control studies including 3370 CAD patients and 3011 controls were included in this meta-analysis. MiR-196a2 rs11614913 polymorphism was not associated with CAD risk in the allelic model (OR=1.02; 95% CI 0.95-1.09; P=0.67). Additionally, no significant results were found in other genetic models. In conclusion, we found that miR-196a2 rs11614913 polymorphism played no role in CAD risk in Asians.

Keywords: MicroRNAs, Coronary artery disease, Genetic, Polymorphism.

Accepted on May 05, 2017

Introduction

MicroRNAs are small non-coding RNAs of approximately 22 nucleotides long [1]. They could regulate target mRNA translation through complementary binding in the 3' untranslated region (3' UTR) of mRNAs [1]. MicroRNAs carry pervasive transcriptional and posttranscriptional regulatory actions relevant to human health and disease, including coronary artery disease (CAD). Labbaf et al. suggest that miR-499-rs3746444-GG is associated with CAD susceptibility and development [2]. Faccini et al. demonstrated that the combination of the three circulating miRNA managed to deliver a specific signature for diagnosing CAD [3]. Liu et al. suggested that miR-208b may serve as a sensitive biomarker for the diagnosis and prognosis of acute myocardial infarction patients [4]. Although some studies have investigated the association between miR-196a2 rs11614913 polymorphism and CAD risk [5-9]. The effect of miR-196a2 rs11614913 polymorphism on CAD susceptibility remains unknown. This meta-analysis aimed to determine this association.

Materials and Methods

Publications search

PubMed and EMBASE were searched to find relevant studies which investigated the association between miR-196a2 rs11614913 polymorphism and CAD risk. The keywords included: “coronary artery disease” or CAD and “miR-196a2”. There was no language and time restriction.

Inclusion and exclusion criteria

Studies were included if they met the following criteria: (1) case–control study; (2) about the association between miR-196a2 rs11614913 polymorphism and CAD risk; and (3) had available genotype frequencies of cases and controls or could be calculated from the paper. Accordingly, the exclusion criteria were (1) duplicate data, (2) abstract, reviews, and animal studies, (3) only included CAD patients.

Data extraction

Two authors extracted the data from included studies independently. The following data were collected from each

study: the first author, year, country, ethnicity, sample size, and numbers of genotype.

Statistical analysis

The strength of association between miR-196a2 rs11614913 polymorphism and CAD risk was estimated by OR with corresponding 95% CI. Q-statistic was applied to investigate heterogeneity among studies. P-value greater than 0.1 for Q test suggested a lack of statistically significant heterogeneity, and the fixed-effect model (Mantel-Haenszel method) was used to calculate pooled ORs. Otherwise, heterogeneity was present and the random-effect model (DerSimonian-Laird method) was more appropriate. Potential publication bias was estimated by symmetry of funnel plot. All statistical tests in this meta-analysis were two-tailed and P-value<0.05 was considered statistically significant unless otherwise noted. Data analysis was performed using Revman 5.1.

Results

Characteristics of the studies

Characteristics the included studies are listed in Table 1. Five case-control studies including 3370 CAD patients and 3011 controls were included in this meta-analysis. All these studies were conducted in Asians.

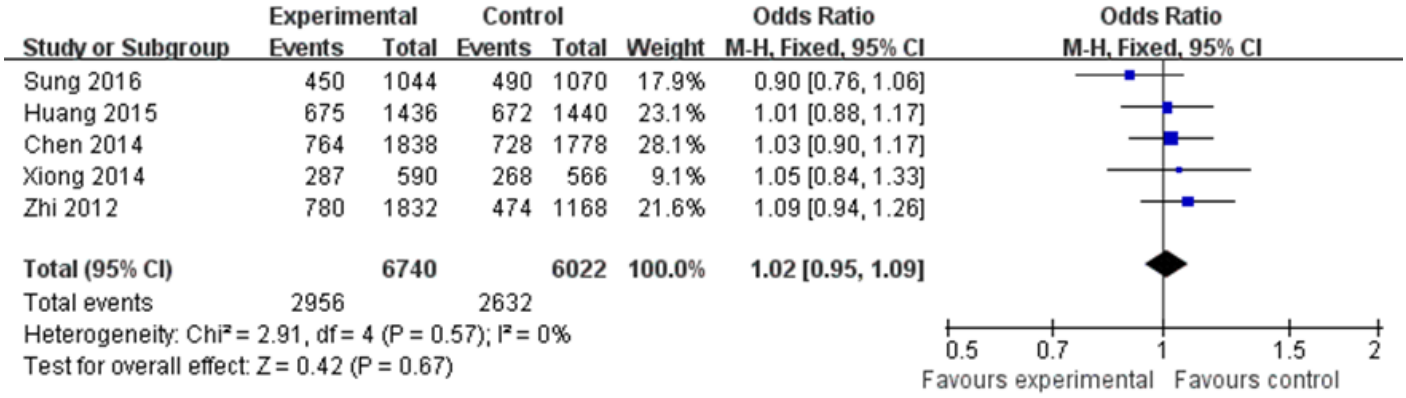

Figure 1. *The association between miR-196a2 rs11614913 polymorphism and CAD risk.*

Table 1. *Characteristics of studies.*

Author	Year	Country	Ethnicity	Cases/Controls (n)	Case			Control		
					CC	CT	TT	CC	CT	TT
Zhi	2012	China	Asian	916/584	155	470	291	98	278	208
Chen	2014	China	Asian	919/889	157	450	312	161	406	322
Xiong	2014	China	Asian	295/283	78	131	86	68	132	83
Huang	2015	China	Asian	718/720	147	381	190	156	360	204
Sung	2016	Korea	Asian	522/535	107	236	179	108	274	153

Meta-analysis

The results of the association between miR-196a2 rs11614913 polymorphism and CAD risk are summarized in Table 2. As shown in Figure 1, miR-196a2 rs11614913 polymorphism was not associated with CAD risk in the allelic model (OR=1.02; 95% CI 0.95-1.09; P=0.67). Additionally, no significant results were found in other genetic models (Table 2). Funnel plot was performed to assess the publication bias of literatures. The shape of the funnel plot did not reveal any evidence of obvious asymmetry (Figure 2).

Table 2. *Meta-analysis results.*

	P heterogeneity	Model	OR (95% CI)	P value
C *vs.* T	0.57	F	1.02 (0.95-1.09)	0.67
CC *vs.* TT	0.53	F	1.14 (1.00-1.29)	0.05
CC *vs.* CT	0.56	F	0.98 (0.87-1.11)	0.74
CC *vs.* TT+CT	0.90	F	0.99 (0.87-1.11)	0.81
CC+CT *vs.* TT	0.11	F	0.98 (0.92-1.05)	0.55

F: Fixed-effects model.

Discussion

The current study used a comprehensive meta-analysis to reveal an miR-196a2 rs11614913 polymorphism and CAD risk. We found that individuals with miR-196a2 rs11614913 polymorphism did not show significant results in the Asians

population. However, this association should be confirmed in Caucasians, since no study using Caucasians was included. The role of miR-196a2 rs11614913 polymorphism in diseases has been studied extensively. Yu et al. suggested that the C allele of the rs11614913 (T>C) SNP of miR-196a2 are associated with a significantly reduced risk of ASD [10]. Hussein et al. found that microRNA-196a2 rs11614913 polymorphism might be associated with asthma severity in our sample of the Egyptian population [11]. Chen et al. suggested that MIR196A2 rs11614913 polymorphism may contribute to an increased risk of hepatopulmonary syndrome in liver cirrhosis patients [12].

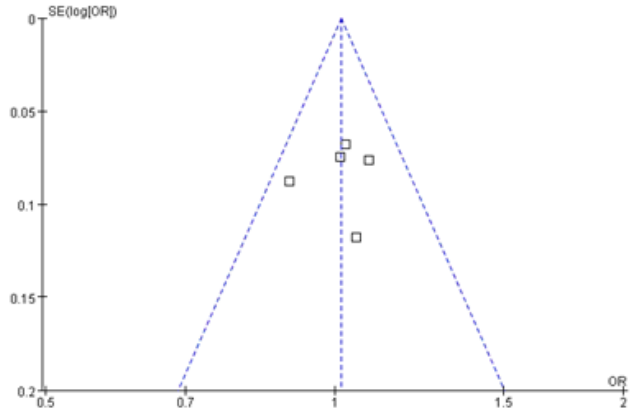

Figure 2. *Publication bias of the association between miR-196a2 rs11614913 polymorphism and CAD risk.*

Some limitations in this meta-analysis should be addressed. First, only published studies were included; it was possible that some relevant published or unpublished studies may have been missed. Second, lacking of the original data of the eligible studies limited the evaluation of the subgroup analyses by gender, age, and other factors. Finally, all the studies were conducted in Asians, no study from other races was included.

In conclusion, we found that miR-196a2 rs11614913 polymorphism played no role in CAD risk in Asians.

Acknowledgment

This work supported by Science and Technology Research Program of Traditional Chinese Medicine of Guangdong Province Hospital of Traditional Chinese Medicine (No. YN2014LN06).

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